Cost of Genetic Counseling and Testing for *BRCA1* and *BRCA2* Breast Cancer Susceptibility Mutations[1]

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Abstract

Counseling and predictive testing are now available for the recently isolated *BRCA1* and *BRCA2* breast cancer susceptibility genes. We examined the societal costs of providing this counseling and testing to women at risk of having a breast cancer susceptibility mutation. Genetic counselors in a research program prospectively monitored the time necessary to provide counseling and results disclosure. A time-motion study was used to determine time spent on phone calls, preparation, and documentation for counseling. Study participants were surveyed to determine travel time and need for dependent care during counseling. The test cost was calculated using the charge for full BRCA1/2 gene sequencing (Myriad Genetics, Inc.) multiplied by a Medicare-based cost-to-charge ratio. Counselors spent an average of 4.2 h providing genetic counseling for women at risk of having a susceptibility mutation. Genetic counseling without testing cost on average $213, whereas counseling, testing, and disclosure of results totaled $2057. A brief physician-based counseling instead of genetic counselor-based counseling would produce only small reductions in total costs. Providing counseling and testing to the study population averaged $8034 per mutation found. The cost of testing and counseling exceeded $2000. The counseling portion of the cost comprised only 16% of the total cost, with the remainder representing costs associated with testing; thus, alternatives to full genetic counseling that shorten counseling time are unlikely to have a large impact on the overall cost of counseling and testing. The cost of detecting a mutation within a population of women is highly dependent on the prevalence of the mutation in the population.

Introduction

Recent advances in molecular genetics have led to the isolation of the *BRCA1* and *BRCA2* breast cancer susceptibility genes (1, 2). Mutations in these genes may account for up to 10% of cases of breast cancer (3) and are observed in a significant proportion of families with multiple cases of breast and ovarian cancer (4). Women who carry a *BRCA1* or *BRCA2* mutation have an estimated 55–85% lifetime risk of breast cancer and a 15–60% risk of ovarian cancer (5–8). Testing for mutations in these two genes is now available commercially.

Information obtained from genetic testing may enable women to make more informed decisions about their medical management. Women who test positive for a *BRCA1* or *BRCA2* mutation have several options for cancer screening and cancer risk reduction, although long-term studies demonstrating the efficacy of these strategies in mutation carriers are not yet available. Women could choose intensive surveillance, initiated at an early age, to maximize the chances of detecting a cancer early (9). On the basis of recent clinical trial data, tamoxifen (10) or raloxifene (11) may be a consideration for breast cancer chemoprophylaxis, although data about the effects of these drugs in mutation carriers are not yet available. However, a recent study demonstrated that oral contraceptive use reduced the risk of ovarian cancer in women with a *BRCA1* or *BRCA2* mutation (12). Women with a mutation may also opt to have a prophylactic mastectomy (13) and/or oophorectomy to decrease the risk of breast and ovarian cancer, respectively. Several decision analyses (14, 15) have suggested that a prophylactic mastectomy may prolong life ~3–4 years for a 30-year-old woman with a *BRCA1* susceptibility mutation.

BRCA1/2 genetic testing also has limitations and risks. Those testing positive may face insurance or employment discrimination (16) and may encounter potentially high medical bills for cancer prophylaxis or surveillance because of their elevated risk of developing cancer. Women testing positive may also have higher levels of distress and anxiety than those testing negative (17). Psychological distress may lead to avoidance of breast cancer screening (18, 19), may interfere with comprehension of personal risk (20), and may impact on treatment or surveillance choices (21). On the other hand, there may be psychological benefits to testing, especially for those persons in high-risk families who test negative (22). However, these individuals may feel falsely reassured that they will not get cancer (16) and therefore may be less likely to adhere to standard screening guidelines.

Counseling can assist women considering *BRCA1/2* testing in making informed decisions about undergoing testing, as well as about possible surveillance and prophylactic options based on the test result. Information about the probability of having a mutation, the risks and benefits of testing, and poten-

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tial options if test results are positive frequently is provided by a genetic counselor or other appropriate clinician (such as oncology nurses, oncologists, or geneticists). Pre- and posttest genetic counseling, given its broad and complex nature, is time intensive. The amount of time and the level of expertise necessary for adequate counseling, although necessary for informed decision making, would suggest that counseling is expensive; however, the cost of providing this counseling has not been well described. We examined the cost of providing genetic counseling for women at high risk for carrying a *BRCA1/2* mutation within the settings of a research study. This study is part of an ongoing project evaluating the costs and outcomes of *BRCA1/2* genetic counseling and testing.

Clinicians and women are interested in breast cancer genetic susceptibility testing (23–25), and counseling and testing are translating from research tools into clinical practice. Clinicians have ordered *BRCA1/2* testing outside of research settings (26), and some managed care organizations are covering part or all of the costs of these genetic tests (27). As counseling and testing become more common, it is important to better understand the costs involved in providing counseling and testing and how these health care costs may be impacted as *BRCA1/2* counseling and testing continue to translate from research to clinical settings. To better understand these costs, we had three goals for this study: (*a*) we examined the cost of counseling and testing in a research program; (*b*) we used sensitivity analysis to examine the costs of a hypothetical alternative program of providing physician counseling and testing, a practice that may occur more frequently as *BRCA1/2* testing translates to clinical practice; and (*c*) we used these costs to calculate the cost necessary to find a mutation by testing women from different populations.

Materials and Methods

Study Population. Eligible subjects included women and men enrolled in the CARE[3] program, a prospective cohort study of BRCA1/2 testing. All study procedures were approved by the Georgetown University Institutional Review Board. Eligible participants had at least a 10% prior probability of carrying a mutation in either *BRCA1* or *BRCA2*, consistent with published recommendations (28). Participants were identified through both physician referrals and self-referrals. After eligibility was determined, participants completed a baseline telephone interview to collect data on family history, medical history, risk factors, and psychological well-being. After providing written informed consent, individuals participated in a pretest counseling session (see below). Those opting for genetic testing provided a blood sample for mutation analyses, and results were disclosed during a subsequent genetic counseling session. Probands, the first individuals in a family to be offered testing, were women with a diagnosis of breast cancer (or in rare cases, men with a diagnosis of breast cancer) or ovarian cancer, often at a young age and in conjunction with a family history of these diseases. If a mutation was identified in the family, then male and female relatives were invited to participate in the program. All genetic counseling and testing were offered free of charge to the participants. Follow-up interviews to assess the outcomes of testing were or will be completed at 1, 6, and 12 months after testing (or declining test results). The present study focuses on data collected at the pretest interview and counseling visits.

[3] The abbreviations used are: CARE, Cancer Assessment and Risk Evaluation; FDR, first-degree relative.

Genetic Counseling Procedures and Content. The majority of participants in the CARE program completed genetic counseling visits with one of two board-eligible or board-certified masters-level genetic counselors; several were counseled by an oncology nurse with training in cancer genetics. Pre- and posttest genetic counseling was a required part of the study for those interested in testing. Individual disclosure sessions were performed with one of the genetic counselors and, in some cases, a medical oncologist. Regardless of the test result, the genetic counselor contacted the participant ~2 weeks after the result was given for an unstructured clinical follow-up telephone call.

The content of the genetic counseling sessions was standardized but not scripted for each participant. The following topics were addressed in the pretest genetic counseling sessions: (*a*) a detailed review of the consultand's medical and family history, including compilation of a multigeneration pedigree; (*b*) an overview of hereditary breast cancer and approach to risk assessment; (*c*) cancer risks associated with *BRCA1* and *BRCA2* mutations; (*d*) autosomal dominant inheritance and implications for relatives according to the pedigree; (*e*) options for medical management, including surveillance and risk reduction; (*f*) the potential benefits, risks, and limitations of testing, including provisions for confidentiality; and (*g*) an exploration of the patient's anticipated response to test results and coping skills, plans for communication of test results, and resources for support. The posttest session included a review of pertinent material from the first session, with a more tailored discussion of cancer risks, medical management options, risks to relatives, and coping strategies. Supportive counseling was provided as needed.

Measures. Data collected for the present analysis included time costs for counselors to provide counseling and costs for participants to receive counseling. The time necessary for a counselor to counsel a patient was derived from two sources. For the first source, face-to-face counseling time was determined by prospectively recording the counseling time for a sample of 191 patients. Time data were recorded using a categorical scale ($<$1 h, 1–1.5 h, $>$1.5–2 h, $>$2–2.5 h, $>$2.5 h). The midpoint of each category was used to estimate the time for each patient; the highest category was assumed to have a time of 2.5 h. For the second source, the counselors' telephone follow-up time and documentation time for counseling and phone calls were determined by monitoring the counselors' activities during a 3-week period. Activities tracked included the time required to provide in-person pretest genetic counseling, disclosure of test results, and telephone follow-up in addition to the time spent preparing for the counseling session and in documenting patient interactions, including genetic counseling summary notes for the chart and the patient. The program counseled both probands and relatives of probands who had known mutations. We based the counselor time costs on the time spent counseling probands; thus, the cost of counseling that we calculate assumes no prior knowledge of mutations in the participant's family.

The time that participants spent traveling to the study site was determined by a written survey administered to 186 women in the study. Time was recorded in categories of $<$10 min, 10–29 min, 30–59 min, 1–2 h, and $>$2 h. Category midpoints were used as the estimated travel time. Participants were asked to specify a time if the highest category was chosen; this value was used if specified, and 2 h was used if the value was not specified. The survey also asked participants whether they needed child or adult dependent care during the time that they were in counseling.

Data Analysis. To determine the resources necessary for providing genetic counseling and testing, we calculated the average national costs as opposed to the charges for providing these services. Costs considered in this analysis include personnel costs, non-personnel-related costs involved in providing counseling and testing, and patient costs of receiving counseling. We divided costs into two categories: those associated with genetic counseling, and the additional costs associated with genetic testing and disclosure of results. All costs are presented in 1998 dollars.

Personnel costs included the costs of the counselor's time and the time of the clerical or receptionist staff. The time spent by the counselor in preparation, documentation, and telephone follow-up was estimated by determining the ratio of these times to the time spent in face-to-face counseling and then multiplying the face-to-face counseling time by these ratios. Cost of the counselor's time for one patient was determined by multiplying the total number of hours that the counselor spent in face-to-face counseling, preparation, documentation, and phone calls by the average hourly wage plus fringe benefit costs for genetic counselors, as determined by a national survey of genetic counselors (29, 30). This survey of 816 genetic counselors was conducted in May 1998. We estimated an hourly wage and fringe rate based on average salary in the United States and assuming that the annual salary and fringe total was based on 2000 working hours per year.

The cost of clerical time was determined by estimate of the counselors, including time to assemble patient materials, type appointment letters, and review materials returned by patients for completeness. This time was multiplied by an average hourly cost based on the median weekly earnings for clerical personnel (31). Counselors' office space necessary for counseling was calculated using the cost to the institution of the counselors' office space, prorated for the time spent providing counseling services to one consultand.

We considered two main costs for the patient in receiving counseling: the costs of the time in counseling, including the travel time to reach the counselor's office; and the costs of providing short-term dependent care (if any) while the patient was at counseling. Time costs were determined using the average sex- and age-specific hourly wage rates provided by the Bureau of Labor Statistics[4] for a woman of the average age of the cohort multiplied by the average counseling and travel times for the participants. Dependent care costs were estimated for those women reporting needing this care by taking the time necessary to receive counseling multiplied by an estimate of $8 per hour.

Costs of testing and disclosure were calculated as follows. Personnel costs to provide testing and disclosure included the cost of the genetic counselor's time to disclose the results to the woman and the cost of a phlebotomist's time to draw blood for genetic testing. Although a medical oncologist previously had been present with the counselor for disclosure of results to those who tested positive for a mutation, the program's current practice is to have the counselor alone provide disclosure; thus, personnel costs included the counselor's time but not an oncologist's time. Phlebotomists were asked to estimate the time necessary to draw blood for genetic testing; this time was multiplied by the average salary plus fringe benefit costs for a phlebotomist at our institution. Participant costs were calculated in a fashion similar to those for the genetic counseling.

Non-personnel costs of testing included cost to the institution for phlebotomy materials and the cost of the test itself. The cost of testing was based on the cost of providing full gene sequencing for *BRCA1* and *BRCA2*; the cost of this test was estimated using the retail charge for commercially available full gene sequencing (Myriad Genetics, Inc., Salt Lake City, UT) using an a cost-to-charge ratio of 0.664:1, which represents the ratio for medical care based on the 1995 Medicare Cost Reports.

We performed two sensitivity analyses to examine changes in our assumptions about the costs involved in counseling and testing. Because the cost of testing was estimated from a retail charge, we first examined the effects of varying the charge-to-cost ratio used to calculate the cost. We then examined the effects of physician counseling instead of genetic counselor-based counseling, using an estimated physician salary of $150,000 per year, plus a 23% fringe benefit rate, to calculate a representative hourly time cost for physician counseling. The cost of physician-based counseling and testing was then calculated as a function of the time spent by physicians compared with genetic counselors.

To examine the costs of screening in different populations, we estimated the cost of counseling and testing that would be necessary on average to find one *BRCA1* or *BRCA2* mutation in these populations. To perform this analysis, we first calculated the number needed to test to find a mutation, defined as the inverse of the prevalence of the mutations in the population of interest. We assumed that counseling and testing would consist of full pretest counseling, as represented by the proband counseling in CARE, and that full gene sequencing would be followed by posttest counseling. Thus, the cost of finding a mutation was calculated by:

$$\text{Cost} = \frac{(\text{Cost}_{\text{counseling}} + \text{cost}_{\text{disclosure and testing}})}{\text{Prevalence}}$$

Testing in some populations may not require full gene sequencing as the initial test. For example, ~90% of Ashkenazi Jews who had a *BRCA1* or *BRCA2* mutation were found in one study to have one of three founder mutations: *185delAG* or *5382insC* in *BRCA1*, or *6174delT* in *BRCA2* (4). In this group, we examined the cost per mutation found for two testing strategies: (*a*) test all women for the three founder mutations and stop if this test is negative; and (*b*) test all women for the three founder mutations, and if the test is negative, then proceed to full gene sequencing. The cost per mutation found for the first strategy was calculated using the charge for testing for these three founder mutations multiplied by the cost-to-charge ratio substituted for the cost of full gene sequencing in the following equation:

$$\text{Cost}_{\text{founder}} = \frac{(\text{Cost}_{\text{counseling}} + \text{cost}_{\text{disclosure and founder testing}})}{\text{Prevalence} \times \text{sensitivity}_{\text{founder testing}}}$$

where the sensitivity of the founder mutation testing is estimated at 0.9 (4). Cost per mutation found for the second strategy was calculated with the following equation:

$$\text{Cost}_{\text{founder}} = \frac{1}{\text{Prevalence}} \times \{(\text{cost}_{\text{counseling}} + \text{cost}_{\text{disclosure and founder testing}}) + [(1 - \text{prevalence} \times \text{sensitivity}_{\text{founder testing}}) \times \text{cost}_{\text{sequencing}}]\}$$

[4] Bureau of Labor Statistics. http://stats.bls.gov/blshome.html.

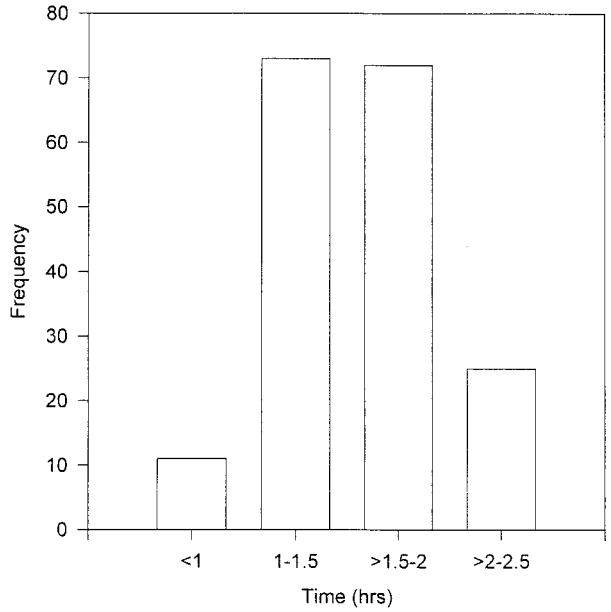

Fig. 1. Distribution of time taken to provide face-to-face genetic counseling to women at risk for carrying a *BRCA1/2* breast cancer susceptibility mutation.

In this scenario, all participants received the cost of founder mutation testing, and those testing negative (represented by the 1 − prevalence × sensitivity term above) also received the cost of full gene sequencing. We assumed that all women would receive only one pretest counseling session and one posttest disclosure.

Results

Cohort Characteristics

Participants in the program had an average age of 47.3 years (SD, 12.2 years); the majority (71%) of the cohort had completed college. Of the 181 participants for whom data on time of counseling were available, 127 (70.2%) were affected by either breast or ovarian cancer. One hundred twenty three participants (68.0%) were probands, and 58 were relatives of probands with known mutations. There were 161 women and 20 men in the study; only 3 of the males were probands. Genetic test results were available for 159 of these participants; 38 (23.9%) tested positive for a known deleterious *BRCA1* or *BRCA2* mutation.

Counseling Costs

The distribution of counseling times for the cohort by cancer status is shown in Fig. 1. On average, the counselors spent 1.63 h (SD, 0.40 h) in face-to-face counseling for each proband in the study, significantly longer than the average 1.33 h (SD, 0.43) spent counseling relatives ($P < 0.0001$, two-tailed t test). For this time spent with a proband, the counselors spent ~0.46 h in phone conversations with the participant and another 2.13 h preparing for and documenting the counseling, for a total time of 4.2 h spent by the counselor to provide counseling for one participant. Costs of counselor time were calculated using a national average of salary plus fringe benefits of $53,755 per year, or an average hourly rate of $26.88 per hour. Using this rate, we calculated a total cost of counselors' time of $119 per proband (Table 1).

Table 1 Costs of genetic counseling and testing for probands

Category	Cost ($)
Counseling costs	
Counselor costs	119
Ancillary personnel costs	7
Participant costs	80
Non-personnel costs	7
Total counseling costs	213
Testing and results disclosure costs	
Counselor disclosure costs	44
Participant costs	72
Phlebotomist cost	7
Phlebotomy material, office space	8
Gene sequencing	1713
Total testing and disclosure costs	1844
Total counseling + testing costs	2057

Table 2 Cost for physician-based counseling and testing

Time spent counseling (min)	% of counselor's time[a]	Cost ($)	Reduction of Cost[b] (%)
41	25	1996	3.0
16	10	1909	7.2
3	2	1863	9.4
20 additional[c]	14.9	2087	(1.5)

[a] Compared with 1.63 h, average time for a genetic counselor to counsel a proband.
[b] Reduction in cost compared with baseline analysis.
[c] Assumes 10 min spent by physician at pretest counseling and at posttest disclosure in addition to the baseline amount of counselor time.

The costs of clerical time and participant time are shown in Table 2. These costs were based on an estimate of 30 min of clerical time necessary for each proband counseled and an average of 5.51 h spent by participants undergoing counseling. An average of 14% of participants needed a caregiver for a child or dependent adult during the counseling session. Non-personnel costs for counseling included the office space for the counseling session.

Testing Costs

The additional costs associated with receiving testing in addition to counseling are also listed in Table 1. Costs included the costs of the phlebotomist's time, estimated by our phlebotomists at 30 min average per person. This estimate encompassed time to complete test requisition forms and delivery of samples. For patients who opted to obtain their test results, an additional 0.61 h (SD, 0.29 h) of face-to-face counseling, on average, was required to disclose the result to the participant. The major cost of testing was the gene sequencing itself, representing 84% of total costs. Costs associated with the pretest counseling and posttest disclosure comprised the remaining 16% of the costs.

Sensitivity Analyses

Charge-to-Cost Ratio. Our baseline analysis assumed a charge of $2580 and a cost-to-charge ratio of 0.664:1. If the cost-to-charge ratio is smaller, representing a greater difference between the charge for the test and the cost of the test, then the cost of the test will be lower. If the charge-to-cost ratio is 0.5:1, then the cost of the test will be $1290 and the total cost of counseling and testing

Table 3 Cost of detecting a *BRCA1* or *BRCA2* mutation

Population	Mutation prevalence (%)	Reference	Cost to detect mutation ($)
CARE[a]	25.6		8,034
Breast cancer 21–44 years[a]	7.2	(46)	28,565
Breast cancer, unselected[a]	2.6	(47)	79,104
United States population[a]	0.14	(48)	1,469,080
Ashkenazi Jews (founder mutations only)[b]	2.4	(49)	23,357
Ashkenazi Jews (founder mutations + full gene sequencing)[c]	2.4	(49)	82,002

[a] Average cost of testing and counseling for women in the population of interest necessary, on average, to have one positive test for a BRCA1 or a BRCA2 mutation, assuming the use of full gene sequencing, and that the test is the gold standard diagnosis of a mutation.
[b] Assuming testing for three founder mutations (185delAG, 5382insC, 6174delT) with no further evaluation if the tests are negative.
[c] Assuming testing for three founder mutations (185delAG, 5382insC, 6174delT) and testing those who test negative with full gene sequencing.

will be $1634, with the cost of the test accounting for 79% of the total cost.

Physician Counseling. Our analysis examined the cost of having genetic counselors provide counseling and disclosure of results. What would happen to the cost of counseling and testing if physicians provided this counseling and disclosure instead of counselors? Table 2 shows the impact on costs of physicians providing counseling as a function of the time spent to provide face-to-face counseling, expressed as a percentage of the time spent by the genetic counselors in this study. Physician counseling, even if much shorter than counseling by a genetic counselor, did not have a large impact on total cost; even if the physician counseling time was 3 min, the total cost of testing and counseling were reduced only 9.4% below the baseline cost. If a physician spent time counseling in addition to the counselors, then the overall costs of counseling and testing increased. For example, if a physician counseled each patient for 10 min during the pretest counseling session and the posttest disclosure, then the overall costs increased by 1.5%.

Cost of Finding a Mutation

The average cost of counseling and testing needed to be performed to detect one susceptibility mutation in various populations is shown in Table 3; we assumed for this analysis that the people tested did not have relatives with known mutations, so the cost was based on the cost incurred for probands. The first four entries in Table 3 reflect women without specific founder mutations; therefore, we based testing costs on full gene sequencing. In our research setting of counseling high-risk participants, the prevalence of a deleterious *BRCA1* or *BRCA2* mutation is 26%; therefore, on average, four participants need to be tested to find one mutation. At the other extreme, given the low prevalence of the mutation in otherwise unselected women in the general United States population, 714 women would need to be tested, on average, to find a single mutation. Using our estimate of the cost of counseling and testing, the average cost of finding a mutation would be approximately $8000 for the high-prevalence CARE sample, but testing unselected women in the United States population would cost approximately $1.5 million to detect a mutation (Table 3).

If the population tested were Ashkenazi Jewish women, otherwise unselected for cancer history, the cost of testing for founder mutations would be approximately $23,000 per mutation found (Table 3); however, this testing will only detect ~90% of the mutations in the population. If testing for founder mutations detected >90% of mutations, than the cost per mutation found would decrease slightly (to a minimum of $21,022 per mutation found if 100% of mutations were detected). Detecting the other 10% of mutations, using full gene sequencing as a confirmatory test for those testing negative for founder mutations, would increase the cost to more than $80,000 per mutation found. Other intermediate strategies could be used for testing Ashkenazi Jewish women, *e.g.*, testing all women for founder mutations, and for those women who have a FDR with breast cancer who test negative, use full gene sequencing as a confirmatory test. Under the assumption that Ashkenazi Jewish women have the same risk of having a FDR with breast cancer as women in the general population and that the relative risk of having a *BRCA1/2* mutation for women is equivalent to the relative risk of developing breast cancer for women with an affected FDR (32, 33), then this strategy would detect ~91.4% of mutations for a cost per mutation detected of $27,670.

Discussion

There are potential benefits to testing individuals at high risk for carrying a *BRCA1* or *BRCA2* mutation. However, there are also substantial costs associated with this testing, exceeding $2000 for the combination of genetic counseling and testing. The major expense for this combination is the genetic test itself, for which we used the estimated cost of full gene sequencing. At present, there are >400 known or suspected deleterious mutations identified for the *BRCA1* and *BRCA2* genes.[5] Many families harbor "private" mutations that have never been reported but are known to be deleterious. Full gene sequencing is considered to be the most sensitive method of detecting these mutations (34). However, in certain populations, a few founder mutations appear to account for the majority of detectable alterations in *BRCA1* and/or *BRCA2*. For example, common founder mutations have been reported in individuals of Ashkenazi Jewish (8), Icelandic (35), or French Canadian (36) descent. Less expensive tests to detect these mutations are available. In addition, in most cases, relatives of an individual with a documented mutation can be tested only for the mutation found in their family. Judicious use of such tests may reduce the overall cost of testing. In addition, if testing becomes more common, economies of scale may reduce the cost of full gene sequencing, *e.g.*, by allowing the tests to be run in larger batches decreasing the labor cost for each test in the batch.

The pretest genetic counseling session represented only 10% of the total cost of counseling and testing. Although counseling is a time-intensive procedure, requiring a total of 4.3 h of the counselor's time, the cost of providing this counseling is small in relation to the cost of the test. Genetic counseling should be considered as part of the informed consent process, and it helps to ensure that individuals make knowledgeable choices about testing. This process maximizes the likelihood that individuals will derive some benefits from testing while minimizing the chances of adverse or unanticipated effects. Moreover, the potential to misinterpret test results exists (37) and could have substantial implications for patients and families. Women may prefer obtaining pretest counseling with a genetic counselor over either an oncologist or a primary care physician, particularly if they desire to discuss psychoso-

[5] Breast Cancer Information Core Database. http://www.nhgri.nih.gov/Intramural_research/Lab_transfer/Bic.

cial issues (38). Given the time-intensive and complex nature of such counseling, it is unlikely that offering such services will be feasible for most physicians, most likely making a referral necessary. We found in this study that physician counseling, even if the counseling provided is much more brief than that provided by a counselor, would not largely impact on the overall cost of counseling and testing. The cost of the test is the largest part of the total cost of counseling and testing, representing 84% of the total, so physician counseling would not result in a large reduction in costs even if much less time was spent by the physicians than by the counselors. In consideration of these findings, we strongly advocate that genetic testing be performed only in conjunction with genetic counseling, performed by a genetic counselor or other specialized provider, consistent with other published recommendations (28, 39).

The average cost of finding a mutation in the population depends on the prevalence of the mutations in the populations. The values in Table 3 represent a large range of costs for finding a mutation; this large range is a consequence of the prevalence in the denominator of the equation to determine the average cost to find a mutation. As the prevalence approaches 0, the cost of finding a single mutation approaches infinity. Although this study examines only costs, not effectiveness, it is unlikely that unselected counseling and testing of women in the general population will be cost-effective because the cost of finding a mutation is so high that it is very unlikely that the benefit produced will justify the cost of counseling and testing. Testing unselected women with breast cancer would cost almost $80,000 per mutation found. Whether testing these women with breast cancer would be cost-effective would depend on the amount of benefit gained by those in whom a mutation is detected.

Testing Ashkenazi Jewish women for three founder mutations is significantly less expensive per mutation found than testing women in the general population with full gene sequencing because of the ability to use a much less expensive test that will detect a majority of mutations and because of the higher prevalence of mutations in the Ashkenazi population. Testing for founder mutations only will miss ~10% of women in the population who have deleterious mutations, however. Whether the increased expense of using full gene sequencing to detect the remaining 10% of mutations is justified by an improvement in outcomes will need further study.

Several caveats should be considered when evaluating our results. The first caveat is that the costs calculated in this study are the costs associated with a research program, and not those of standard clinical practice. Although *BRCA1* and *BRCA2* gene testing is still used as a research tool, the use of testing and counseling is also translating into routine clinical practice. Because providing testing is a major portion of the costs, we do not expect the overall costs of counseling plus testing to change significantly in clinical practice unless the type of test used were to change. In this study, we are interested in examining the resource utilization (as measured by health care dollars) necessary to provide counseling and testing; thus, we use costs of the services in this analysis rather than charges for the providing the services. Retail charges for testing and counseling services will be larger than the costs reported in this study. We have used expert opinion to estimate time costs for ancillary personnel, including secretarial and phlebotomist time, but any misestimation is unlikely to significantly influence the results because the total of these costs represents <1% of the cost of counseling and testing. Our value used for the cost of full gene sequencing is an estimate based on a model using commercial testing. The cost of producing a product in private industry is generally not a matter of public record, so we are unable to provide an exact accounting of this cost. To estimate, we used an approximate governmental cost-to-charge ratio. The estimate is similar to an accounted cost of full gene sequencing of the *COL2A1* gene (40).

The second caveat is that our study evaluated counseling at only one location; content and delivery of counseling may differ at other locations, resulting in differing costs. Although the content of genetic counseling for hereditary breast cancer is likely to have similar components in a clinical setting (29), the risk level of the patient, sociodemographic factors such as education level, and protocols of individual centers may vary. For example, some centers have designed their clinics such that patients are seen by a multidisciplinary team that includes medical onocologists, genetic counselors, nurses, and psychologists (41–43). In some cases, group sessions may be conducted for pretest education (22); however, disclosure of test results should take place on an individual basis.

The final caveat is that although we considered the costs of the counseling and testing, the benefits are not fully described. Thus, although we can describe the costs of counseling and testing, we cannot estimate the changes in health outcomes, such as survival or health-related quality of life attributable to counseling and testing in this analysis. Decision models would suggest that in those with a *BRCA1/2* mutation, prophylactic surgery may be beneficial (14, 15, 44, 45), and that testing some high-risk women will improve their outcomes if they make decisions about prophylactic surgery based on their test results (45).

In conclusion, genetic counseling and testing are associated with significant costs. If testing is considered, detailed accounting of the risks and benefits should be provided to the consultand; this counseling can be performed for a fraction of the cost of the test itself. Whether the costs of counseling and testing of women at risk for a mutation are justified by the benefits of these interventions has yet to be determined and will be the subject of future work.

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